REMARKS

Claims 1-5, 13 and 16-29 are pending in the application. Claims 1-5 have been amended and claim 13 has been canceled in view of the amendment to claim 1. Claims 16-29 are withdrawn from consideration as being drawn to a non-elected invention. Upon entry of the present Amendment, claims 1-5 and 16-19 will be pending.

Support for the amendments can be found throughout the specification and claims as originally filed. *No new matter has been added.* The amendments presented herein should in no way be construed as an acquiescence to any of the Examiner's rejections and were made solely in the interest of expediting prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Finally, Applicants respectfully note that the present application is now being handled by the new attorneys of record.

Information Disclosure Statements

At page 2 of the Office Action dated March 28, 2007, the Examiner acknowledged that the Information Disclosure Statement and corresponding PTO-Form 1449 filed by Applicants on September 22, 2004 have been considered. However, Applicants respectfully note that the Examiner has not initialed Reference 28 (*i.e.*, Cookson *et al.*, "Alchemy for Asthma," *Nature Medicine Vaccine Supplement* (1988); 4:550-551). Accordingly, Applicants respectfully request that the Examiner initial this reference on the PTO-Form 1449 to indicate that it has been considered. For the Examiner's convenience, Applicants submit herewith an additional copy of Cookson *et al* (enclosed as Appendix A).

Additionally, Applicants submit herewith a Supplemental Information Disclosure Statement and corresponding PTO-Form SB/08 and respectfully request that the Examiner consider and initial the cited references.

Acknowledgment of the Examiner's Withdrawal of Prior Objections/ Rejections

In the present Office Action, the Examiner did not specifically acknowledge withdrawal of the following rejections: (a) the objection to the specification under 37 C.F.R. § 1.821(d) for failing to provide sequence identifiers for each individual sequence and (b) the rejection of

claims 1, 4-5 and 13 as being anticipated by Hoyne *et al.* (*Int. Immunol.* 1996 Mar;8(3):335-42). However, these objections and rejections are not raised in the present Office Action. Therefore, Applicants respectfully assume that they have been withdrawn, and would appreciate confirmation of such by the Examiner.

Rejection of Claims 1-5 and 13 Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 1-5 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner is of the opinion that it would require undue experimentation "to identify any and all peptides and peptide variants that would be MHC Class II restricted as recited with the claimed functional characteristics." Additionally, the Examiner cites several references to suggest that allergen immunotherapy as a whole is unpredictable and asserts that

> [s]ince altered peptide ligands are encompassed by the instant claim recitations (peptide derived from the allergen) and may also be presented by MHC II molecules in the patient, it stands to reason that responses generated therefrom are unpredictable to generate desensitization.

From the outset, Applicants respectfully note that claim 13 has been canceled in view of the amendment to claim 1. Therefore, this rejection is moot as applied to this claim.

With respect to claims 1-5, Applicants respectfully traverse this rejection. The claims, as amended, do not encompass "any and all peptides and peptide variants" as objected to by the Examiner. Instead, they encompass isolated peptides from known allergens having defined functional and structural features. Specifically, claim 1, as amended, is drawn to a method of inhibiting an allergic reaction to a polypeptide allergen in an individual comprising administering to the individual *an isolated peptide* from the allergen, wherein the peptide possesses *particular functional features* (*i.e.*, the ability to bind a particular MHC Class II molecule possessed by the individual and the ability to induce a late phase response in the individual), and *particular structural features* (*i.e.*, the peptide includes a T cell epitope of a known protein allergen sequence and is 5 to 50 amino acids in length). Accordingly, the breadth of the claims are limited to a particular, well-characterized condition to be treated (*i.e.*, an allergic response) by using particularly defined peptides.

As described in detail below, one of ordinary skill in the art could have identified the peptides encompassed by the claimed methods having the particularly claimed structural and

functional features, without undue experimentation, based on the teachings in the specification and knowledge available in the art.

At the time the present application was filed, it was well within the skill of the art to generate a multitude of peptides from a known protein. For example, Geysen *et al.* (PNAS, 81, 3998-4002 (1984) (enclosed as Appendix B)) describe a method, subsequently referred to as "the pin method" or "the Pepscan method," that allows for the rapid, concurrent synthesis on polyethylene rods of hundreds of peptides of sufficient purity for use in ELISAs. Geysen *et al.* used these peptides to map epitopes of foot-and-mouth disease virus coat protein involved in antibody binding. In a later paper, Geysen *et al.* state that "The current methodology requires only basic skills in organic chemistry, and can be used to synthesize more than 2000 peptides (hexapeptides) per 10 working day." They further state that their group "presently tests about 4000 peptides each working day." (Geysen *et al.*, J. Immunol. Methods, 259-274 (1987) (enclosed as Appendix C)).

Further, numerous genetic manipulations for producing peptides from a known protein sequence were commonplace in the art at the time the present application was filed. Relevant techniques include, for example, the use of restriction enzymes to generate fragments of a nucleic acid molecule encoding the protein of interest; the use of timed exonuclease III and/or Dnase I digestions of a nucleic acid molecule encoding the protein of interest, and the use of the polymerase chain reaction to generate precise fragments of the open reading frame encoding the protein of interest. All of these techniques were being employed at the time of filing and described in the literature (see, for example, Methods in Molecular Biology, vol. 66, Epitope Mapping Protocols (1996) (enclosed as Appendix D))..

Methods of identifying peptides having the particularly claimed functional features were also known. For example, as taught in the present specification at page 7 (lines 15-28) "binding to the given MHC Class II molecule [*i.e.*, possession of a functional T-cell epitope] may be demonstrated directly using suitable samples from the patient...[and] can readily be determined in vitro using methods well known in the art...including the PCR-based methods..." (see, *e.g.*, Olerup & Zetterquist (1992) Tissue Antigens 29:225-235 (enclosed as Appendix E)). Additional methods for identifying T-cell epitope-containing peptides previously known in the art include, for example, Van der Zee *et al.* (Eur. J. Immunol. 19:43-47 (1989) (enclosed as Appendix F)). Specifically, Van der Zee *et al.* modified the Pepscan method (described above) so that the synthetic peptides could be released from the solid phase support, making them available for T

cell stimulation assays. Van der Zee *et al.* used this modified technique to finely map a T-cell epitope in the mycobacterial 65 kDa heat shock protein. Likewise, Maeji *et al.* used the Pepscan methodology to map T cell epitopes of tetanus toxin (Maeji *et al.* J. of Immunol. Methods 134: 23-33 (1990) (enclosed as Appendix G)). In addition to the Pepscsan method, Houghten taught a method for synthesizing large numbers of peptides on standard, amino acid resin that was sealed in packets (the "teabag" method). (Houghten, R.A. (1985) PNAS, 82, 5131-5135 (enclosed as Appendix H)). Oftung *et al.* utilized the method of Houghten to map human T cell epitopes on the Mycobacterium tuberculosis 65-kilodalton protein antigen. (Oftung *et al.* (1988) J. Immunol 141 2749-54 (enclosed as Appendix I)).

As further taught in the present specification, "[w]hether or not a particular peptide can give rise to a LPR [late phase response] can be determined used methods well known in the art..." (see, *e.g.*, Cromwell *et al.*, "Provocation tests and measurements of mediators from mast cells and basophils in asthma and allergic rhinitis," In: Handbook of Experimental Immunology (4) Chapter 127, Editor: Weir D M, Blackwell Scientific Publications, 1986 (enclosed as Appendix J)).

Based on at least the foregoing, one of ordinary skill in the art could have identified the peptides encompassed by the claimed methods without undue experimentation. Moreover, one of ordinary skill could have predictably used such peptides to practice the claimed method without undue experimentation based on knowledge available in the art in combination with the teachings in Applicants' specification. For example, Applicants teach art-known techniques for administering the peptides (see page 35, lines 5-9), exemplary dosages (see page 36, line 11 through page 37, line 25), and particular formulations suitable for administration (see page34, line 24 through page 36, line 9). Accordingly, the presently claimed methods are fully enabled by the specification and knowledge available in the art.

Further, with respect to the Examiner's assertion that Francis *et al.* (*Curr. Opin. Allergy Clin. Immunol.* 2005 Dec;5(6):537-43) and Kinnunen *et al.* (*J. Allergy Clin. Immunol.* 2007 Apr;119(4):965-72), cast doubt on the predictability of the presently claimed methods, Applicants respectfully refer to the enclosed Declaration by Dr. Mark Larche. As described by Dr. Larche in the enclosed Declaration, the unfavorable results of the single vaccine trial described on page 538 of Francis *et al.* could have been due to any number of outside factors and do not negate the numerous successful studies described in Francis *et al.* or the general success of peptide immunotherapy as a whole. Further, as also described in the enclosed Declaration,

contrary to the Examiner's assertion, Kinnunen *et al.* do not teach that altered peptides are unsuitable for the general treatment of allergies. Notwithstanding, Applicants respectfully note that the claims, as amended, do not include "altered peptides", but instead encompass isolated peptides from known allergens having defined functional and structural features (as discussed above).

In view of the foregoing, it is clear that Applicants' disclosure, in combination with the state of the art at the time the application was filed, is more than sufficient to enable one of skill in the art to make and use the claimed invention. As such, Applicants respectfully submit that pending claims are fully enabled under 35 U.S.C. §112, first paragraph and request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-5 and 13 Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 1-5 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserts that

> the specification has not adequately described a correlation between function (desensitization, induces late phase response) and structure responsible for desensitization and induction of late phase response such that one of ordinary skill in the art would have known what peptides encompassed by the claims could be generated to have the disclosed functions.

Applicants respectfully note that claim 13 has been canceled in view of the amendment to claim 1. Therefore, this rejection is moot as applied to this claim.

With respect to claims 1-5, Applicants respectfully traverse this rejection and submit that the written description provided in Applicants' specification more than reasonably conveys to the skilled artisan that Applicants were in possession of the presently claimed methods for the following reasons.

As discussed above, the peptides encompassed by the claimed methods possesses *particular functional features* (*i.e.*, ability to bind a particular MHC Class II molecule possessed by the individual and induces a late phase response in the individual), and *particular structural features* (*i.e.*, the peptide includes 5 to 50 amino acids of a known protein allergen sequence).

It is firmly established that a patent specification need not describe information that was well known in the art to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Indeed, the written description requirement varies with the nature and scope of the

invention at issue, and with the scientific and technologic knowledge already in existence. In *Capon v. Eshhar,* 418 F.3d 1349, 1357 (Fed. Cir. 2005) (hereinafter "*Capon*"), the Federal Circuit explained that "[p]recedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a *variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.* Id. at 1359 (emphasis added)." Accordingly, if the art is mature, less written description is required.

Specifically, in *Capon*, the claims at issue were drawn to DNA molecules encoding chimeric cell-surface receptor proteins made up of two portions having art-recognized (known) amino acid and nucleotide sequences. The Federal Circuit vacated the Board of Patent Appeals and Interference's decision invalidating these claims for lack of written description on the grounds that the sequences of the claimed chimeric DNA molecules were not explicitly disclosed in specification. The Federal Circuit held that the written description requirement did not require recitation of the nucleotide sequence of the claimed DNA in the specification because the sequence was already known in the field.

The facts of *Capon* parallel those of the present application. Similar to *Capon*, Applicants should not be required to describe each and every peptide encompassed by the claimed methods, since techniques for generating and identifying peptides having the particularly claimed structural and functional features were well known in the art at the time of filing the present application. As discussed in detail above with respect to the enablement requirement, numerous techniques and procedures for generating peptides from a known protein sequence were commonplace in the art. Moreover, techniques for testing whether a given peptide had the particularly claimed functional features (*i.e.*, ability to bind a particular MHC Class II molecule possessed by the individual and the ability to induce a late phase response in the individual), were also routine in the field of peptide immunotherapy.

Accordingly, in view of the standard articulated in *Capon* that less written description is required in a mature, predictable field (such as peptide immunotherapy), in combination with the numerous teachings in Applicant's specification and knowledge available in the art at the time of filing, the present application provides more than adequate written description for the presently claimed methods. Accordingly, the requirement of 35 U.S.C. § 112, first paragraph for written

description has been satisfied and Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-5 and 13 Under 35 U.S.C. § 102(b) – Novelty

Claims 1-5 and 13 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 94/24281 as evidenced by Tovey *et al.* (*J. Allergy Clin. Immunol.* 2008 Jul;122(1):114-8). The Examiner relies on WO 94/24281 as teaching a method of desensitizing a patent to a Der p I or Der p II dust mite polypeptide allergen which involves administering to a patient one or more peptides derived from the allergen, wherein the peptide is 5-50 amino acids long and is not a Fel d I-derived peptide. The Examiner relies on Tovey *et al.* as an evidentiary reference to show that all humans have been previously exposed to dust mite allergens and, as such, the generation of a late phase response in a patient is inherent.

Applicants respectfully traverse this rejection. However, to expedite prosecution, Applicants have amended the claims such that they no longer read on peptides from dust mites, thereby obviating this rejection. Further, the claims have been amended to specify an "isolated" peptide and, thus, do not encompass allergens which occur naturally. Accordingly, Applicants respectfully request that this section 102(b) rejection be reconsidered and withdrawn.

CONCLUSION

In view of the above amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

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